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TITLE: Supplemental Perioperative Oxygen to Reduce Surgical Site Infection after High-Energy Fracture Surgery

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14. ABSTRACT Our study is a multi-center prospective randomized treatment trial investigating if supplemental perioperative oxygen use will reduce surgical site infection after surgery on fractures with a high risk of infection. The study utilizes the DOD-funded Major Extremity Research Consortium (METRC). The study population is calcaneus, pilon, and tibial plateau fractures. During the first year we created a protocol committee, designed and approved the protocol and CRFs, obtained IRB approval. We have enrolled 1000 patients at 20 centers. Follow up rate has been strong with 91% at 12 months. Based on feedback from the DSMB we have increased our enrollment goal to 1200 and anticipate achieving this in the next 6 months.

15. SUBJECT TERMS
Supplemental perioperative oxygen, surgical site infection, fracture fixation complications

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1. INTRODUCTION:

The overall scope of this project is to address the treatment of high-energy military fractures, which has historically been shown to have poor outcomes and continues to be associated with high rates of infection. Perioperative oxygen has been studied in several thousand general surgery patients and shows promise to reduce surgical site infection in these patients. This technique might have tremendous public health consequences as it is already available in all operating rooms throughout the world and has almost no cost or risks. Outside of a pilot study performed at our institution (Reference 1), this technique has not been investigated in high energy fracture patients that are at such risk for surgical site infections. Our study is a well powered multi-center randomized controlled trial investigating the use of supplemental perioperative oxygen to address the problem of infection in these at risk patients. Our hypothesis is that the use of supplemental perioperative oxygen for fractures at high risk for infection will reduce infection rates and therefore improve outcomes compared to treatment without this technique. The study population is patients with high energy tibial plateau, pilon (distal tibia), and calcaneus fractures. The results of this trial have the potential to reduce surgical site infection within both the military and civilian sectors and therefore improve patient outcomes from these potentially devastating injuries.

2. KEYWORDS:

Supplemental perioperative oxygen, surgical site infection, fracture fixation complications, complication reduction, pilon fracture, calcaneus fracture, tibial plateau fracture

3. OVERALL PROJECT SUMMARY:

The fifth year of the grant built on the success of the first four years. During the second year we the study and began enrolling. In the fifth year we are now enrolling at 20 sites and have enrolled the original goal of 1000 patients (1000th patient enrolled in mid October 2017, 48% of those eligible) Almost 500 patients have followed up to date. Follow up rates have been strong as the 3 month follow up rate is 93%. The rate is 88% at 6 months and 91% at 12 months. Based on feedback from our DSMB and we have decided to increase the enrollment goal another 200 patients which should take us 6 more months. The study is performing well and there are no known barriers to study success at this time.

Specific Aim #1 Compare the proportion of surgical site infections within 6 months in patients treated with Supplemental Perioperative Oxygen compared to those treated without Supplemental Perioperative Oxygen.

1.1.Finalize Study Protocol

1. 1.1 Protocol Committee Creation

The Protocol Committee was successfully defined and formed during the first quarter of year one in keeping with METRC (Major Extremity Trauma Research Consortium) guidelines as described in previous reports. The committee for this study is detailed in Appendix 1. We designed to the committee to make sure it represents leaders in all fields that the study will involve. The committee for this study encompasses:

1. The P.I.
2. Orthopaedic Trauma Surgeons, from METRCg sites.
3. Infectious Disease Attendings, with expertise in orthopaedic infections
4. Two Anesthesiologists
5. Two PACU nurses
6. One Research Coordinators from Participating sites
7. One Research Coordinator from the PI's site
6. Two METRC Coordinating Center Staff (expertise in study design)
7. One METRC PI (Castillo)

The Protocol Committee members was defined, invited, and formed during the first quarter.

1.1.2. Protocol Development

***Protocol Design*:**

During the first year the protocol was designed and finalized (included in Appendix 2 of first year report).

Protocol Approval History:

***Protocol Committee Approval*:** The final protocol for IRB submission was approved by the protocol committee on January 2013.

***METRC Steering Committee Approval*:** The protocol was circulated to the entire METRC Steering Committee. The final protocol for IRB submission was unanimously approved by METRC steering committee vote on February 2013.

1.2 Finalize/Adapt/Test Study Materials

CRF/SOP Development

CRF/SOP Design The Case Report Forms (CRFs) were developed in parallel to the protocol development along a similar timeline, leveraging previous METRC infrastructure to maintain uniformity with other METRC projects and leveraging on our experience with our pilot study (Reference 1) and other METRC studies.

CRF's were included in the annual report of year 1.

IRB Submission: The CRFs have been part of the IRB submission at sites that require it.

1.3 Train Study Coordinators

Study coordinator training occurred through both online live training (September 6, 2013) and in person training at the national meeting (October 9, 2013).

The presentation materials for local site training of anesthesia and recovery room nursing staff have been developed and completed by a subgroup of the protocol committee. This training will occur at each site just prior to first patient enrollment.

Additionaly the PI and key personell from the protocol committee and METRC coordinating center contact each site and the local investigators for phone meetings once study enrollment begins to ensure that all questions are answered and to address any site specific issues.

1.4 IRB Approval at First Site (Milestone #1)

This task was accomplished in year one as detailed in prior reports.

IRB Approval at PI Site: The IRB submission was approved by University of Maryland School of Medicine on June 3rd 2013. A very minor modification required by the DOD IRB required IRB resubmission and this modification approval was received on October 15, 2013.

IRB Approval at METRC CC: The original IRB submission was approved by Johns Hopkins April 3, 2013. Revised protocol was approved on September 15, 2013 after modification for aforementioned minor changed required by DOD.

IRB Approval at DOD: DOD approval was obtained October 28, 2013.

DOD IRB Approval of PI Site: Pending

Assuming a relatively rapid approval of our IRB approved protocol by DOD, we are well positioned to begin enrollment at the first site soon.

1.5 IRB Approval at All Sites

The process of IRB approval at other sites has proceeded well in the past year. Of the 19 participating sites, 12 have local and DOD IRB approval and are currently enrolling, 4 are certified to begin enrollment, and 3 are in various stages of IRB approval process. We anticipated IRB approval at all sites in next quarter.

1.6 Enroll First Patient (Milestone #2)

The first milestone was accomplished during this last year on January 7, 2014 at the PI's site.

1.7 Enrollment

Enrollment is underway and proceeding well. We have enrolled all 1000 patients of our original sample size to date (48% of eligible) with a 91% 12 month follow up rate (see Appendix 2). As anticipated, site enrollment peaked at a pace of nearly 600 per year (see Appendix 2); once the VANCO study completed enrollment. This is because the METRC VANCO study competes for these same patients and runs at 35 METRC sites. The plan has always been to complete VANCO enrollment first (which was accomplished) and then immediately switch those sites back to OXYGEN (which was also accomplished). The high volume sites switching to OXYGEN allowed us to quickly reach a high enrollment rate and will allow us to enroll these extra patients within 6 months.

Based on recommendations of our DSMB we are planning to enroll 200 additional patients to increase our power based on lower than expected event rates in the control group.

2. Specific Aim #2 Compare bacterial species and antibacterial sensitivities of the bacteria in the patients who develop surgical site infections in study patients treated with Supplemental Perioperative Oxygen compared to those treated without Supplemental Perioperative Oxygen.

2.1 Finalize Study Protocol

The general progress and timing of the study protocol creation regarding specific aim #2 are identical to those described in specific aim above in section 1.

2.2 Finalize/Adapt/Test Study Materials

The general progress and timing of the creation of the study materials regarding specific aim #2 are identical to those described in specific aim above in section 1.

2.3 Train Study Coordinators

Identical to specific aims #1 as described above in section 1.

2.4 IRB Approval at First Site (Milestone #1)

Identical to specific aims #1 as described above in section 1.

2.5 IRB Approval at All Sites

Identical to specific aims #1 as described above in section 1.

2.6 Enroll First Patient (Milestone #2)

Identical to specific aims #1 as described above in section 1.

2.7 Enrollment

Identical to specific aims #1 as described above in section 1.

3. Specific Aim #3 Validate the previously developed risk prediction model for the development of surgical site infections after fracture surgery (Reference 2,3,4,5).

3.1 Interim Analysis/Final Analysis

One of the specific aims of this project is to validate a model to predict risk for infection after orthopaedic fracture surgery. We are basing this off our previous work and have done an

analysis of our pilot data (different treatment but similar patient population [1]) to analyze risk factors for infection. This has now been published in J Trauma [2,3,4,5].

This work can only begin after patient follow up has been completed.

4. Specific Aim #4 Measure and compare resource utilization and cost associated with surgical site infection in study patients treated with Supplemental Perioperative Oxygen compared to those treated without Supplemental Perioperative Oxygen

4.1 Interim Analysis/Final Analysis

One of the specific aims of this project is to evaluate this technique in terms of cost. Determining the "cost effectiveness" of this technique will be important in determining if it is appropriate for broader distribution. Our hypothesis is that it is such a low cost technique that even modest decreases in infection rate will be very cost effective.

This work can only begin after patient enrollment has been completed. The DSMB recommended enrolling 200 more patients based on analysis of the control event rate.

4. KEY RESEARCH ACCOMPLISHMENTS:

Our key research accomplishments during year two of the grant include:

1. 26 study sites enrolled at least 1 patient.
2. Original goal of 1000 patients enrolled (Mid October, 2017)
3. 91% follow-up rate at 12 month follow up.
4. No cost extension for 2 years (EWOF) applied for and obtained. This will allow us to enroll an additional 200 patients and follow them for 1 year.
5. Study is on pace to complete patient enrollment in a reasonable time frame.
6. Protocol paper paper published [6].

5. CONCLUSION

We believe that this project has significant potential to impact wounded warriors' and civilians' outcomes by reducing the rate of surgical site infection if our primary hypothesis is confirmed.

This past year demonstrates that we are clearly on track for study success. We are now enrolling patients at a high rate and with high follow up rates. There are no barriers to study success and we look forward to finishing enrollment in a reasonable time frame.

6. PUBLICATION, ABSTRATS, AND PRESENTATIONS

Protocol paper published.

7. INVENTIONS, PATENST, AND LICENSES

Nothing to report

8. REPORTABLE OUTCOMES

Nothing to report

9. OTHER ACHEIVEMENTS

Nothing to report

10. REFERENCES:

1. Stall A, Paryavi E, Gupta R, Zadnik M, Hui E, O'Toole RV, "Perioperative supplemental oxygen to reduce surgical site infection after open fixation of high-risk fractures: A randomized controlled pilot trial" J Trauma Acute Care Surg 2013 Volume 75 Number 4 657-63.

2. Paryavi E, Stall A, Gupta R, Zadnik M, Hui E, Castillo RC, Scharfstein DO, O'Toole RV "A Predictive Model for Perioperative Assessment of Infection Risk in High Energy Lower Extremity Injuries" Podium Presentation at American Academy of Orthopaedic Surgeons, San Diego, CA, 2011.

3. Paryavi E, Stall A, Gupta R, Zadnik M, Hui E, Castillo RC, Scharfstein DO, O'Toole RV "A Predictive Model for Perioperative Assessment of Infection Risk After Surgery for High Energy Lower Extremity Injuries: Development of the Risk of Infection in Orthopaedic Trauma Surgery (RIOTS) Score" Podium Presentation at OREF Chesapeake Region Resident Research Symposium, December 2010.

4. Paryavi E, Stall A, Gupta R, Zadnik M, Hui E, Castillo RC, Scharfstein DO, O'Toole RV "A Predictive Model for Perioperative Assessment of Infection Risk in High Energy Lower Extremity Injuries" Poster Presentation 26th Annual Meeting of Orthopaedic Trauma Association, Baltimore, MD, October 2010.

5. Paravi E, Stall A, Gupta R, Scharfstein DO, Castillo RC, Zadnik M, Hui E, O'Toole RV, "Predictive model for surgical site infection risk after surgery for high-energy lower extremity fractures: Development of the Risk of Infection in Orthopedic Trauma Surgery Score" J Trauma Acute Care Surg 2013 Volume 74 Number 6 1521-27.

6. O'Toole RV, Joshi M, Carlini AR, Sikorski RA, Dagal A, Murray CK, Weaver MJ, Paryavi E, Stall AC, Scharfstein DO, Agel J, Zadnik M, Bosse MJ, Castillo RC, METRC "Supplemental Perioperative Oxygen to Reduce Surgical Site INfeciton Afer High-Energy Fracture Surgery (OXYGEN Study) J Orthop Trauma 2017 Apr;31 Suppl 1: S25-S31.

11. APPENDICES:

Appendix 1. Protocol Committee

First Name	Last Name	Role	Site	
Robert	O'Toole	PI (Surgeon)	UMD	ROtoole@umoa.umm.edu
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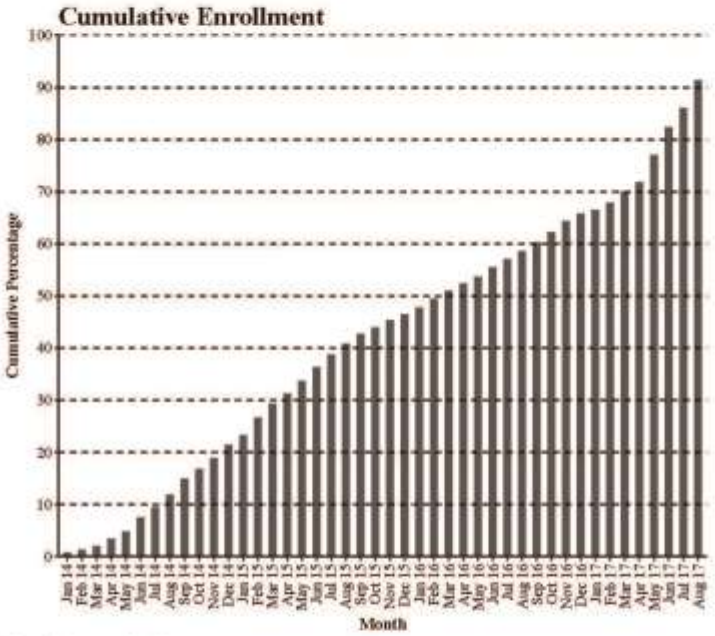
Appendix 2. Oxygen Monthly Report (Oct 1, 2017)

OXYGEN Monthly Report

Supplemental Oxygen to Reduce Surgical Site Infection

Data as of October 1, 2017



Enrollment Updates

- There are 26 centers participating in this study (all centers are certified).
- 3779 patients have been screened for eligibility and of these, 2009 (53%) were eligible.
- 961 (48% of eligible) were consented and enrolled.
- We have now reached 96% of our total enrollment goal (see figure)
- 477 patients have completed the study.

Screening and Enrollment Summary
All Participating Sites

Facility	Days Certified	Expected Screened	Number Screened	Number Enrolled	Enrolled This Month	Completed	Discontinued
ALL			3779	961	51	477	67
UWA	1020	790	476	196	1	80	13
UMD	1381	840	626	163	14	89	2
HOU	1315	458	314	103	8	46	7
CMC	1332	463	578	100	4	49	3
HRV	1119	-	150	72	1	41	9
VMC	1208	404	245	54	5	35	2
MTH	1129	436	302	51	1	22	3
AGY	1179	-	70	33	0	22	7
ESK	1110	-	111	22	1	14	2
BMC	1189	254	120	21	0	16	4
USF	1154	234	66	18	1	3	1
MIN [1]	812	138	63	18	0	14	0
YRK	1150	-	20	17	0	13	3
PEN	1075	-	43	15	1	4	6
UOK	1035	181	73	13	0	7	3
NSD	1172	39	12	11	2	6	0
SPC [2]	902	227	77	10	0	9	1
COR	394	-	64	10	0	0	0
LUB	111	-	9	9	5	0	0
UKY	-	-	8	8	6	0	0
WFU	1305	536	243	7	0	7	0
CAM	667	-	80	3	0	0	1
MET	97	32	23	3	0	0	0
DAR	94	-	2	2	0	0	0
STN	237	-	2	1	0	0	0
HAC	55	-	1	1	1	0	0
PSU	107	24	1	0	0	0	0
CED	-	-	-	-	-	-	-

Monthly Table 1
Number of Subjects Screened [3], Eligible, Enrolled, and Not Enrolled
Cumulative by Site

Facility	Days Certified [4]	Expected Screened	Number Screened	Number Eligible	Among those Eligible (% Eligible)		
					Number Enrolled	Number Refused	Number Not Enrolled
ALL			3779	2009 (53%)	961 (48%)	268 (13%)	780 (39%)
AGY	1179	-	70	41 (59%)	33 (80%)	5 (12%)	3 (7%)
BMC	1189	254	120	28 (23%)	21 (75%)	2 (7%)	5 (18%)
CAM	667	-	80	64 (80%)	3 (5%)	14 (22%)	47 (73%)
CMC	1332	463	578	354 (61%)	100 (28%)	68 (19%)	186 (53%)
COR	394	-	64	29 (45%)	10 (34%)	2 (7%)	17 (59%)
DAR	94	-	2	2 (100%)	2 (100%)	0 (0%)	0 (0%)
ESK	1110	-	111	39 (35%)	22 (56%)	17 (44%)	0 (0%)
HAC	55	-	1	1 (100%)	1 (100%)	0 (0%)	0 (0%)
HOU	1315	458	314	162 (52%)	103 (64%)	23 (14%)	36 (22%)
HRV	1119	-	150	126 (84%)	72 (57%)	41 (33%)	13 (10%)
LUB	111	-	9	9 (100%)	9 (100%)	0 (0%)	0 (0%)
MET	97	32	23	6 (26%)	3 (50%)	0 (0%)	3 (50%)
MIN	WFS	138	63	28 (44%)	18 (64%)	1 (4%)	9 (32%)
MTH	1129	436	302	101 (33%)	51 (50%)	7 (7%)	43 (43%)
NSD	1172	39	12	11 (92%)	11 (100%)	0 (0%)	0 (0%)
PEN	1075	-	43	27 (63%)	15 (56%)	8 (30%)	4 (15%)
PSU	107	24	1	0 (0%)	-	-	-
SPC	WFS	227	77	20 (26%)	10 (50%)	4 (20%)	6 (30%)
STN	237	-	2	2 (100%)	1 (50%)	0 (0%)	1 (50%)
UKY	-	-	8	8 (100%)	8 (100%)	0 (0%)	0 (0%)
UMD	1381	840	626	381 (61%)	163 (43%)	32 (8%)	186 (49%)
UOK	1035	181	73	38 (52%)	13 (34%)	10 (26%)	15 (39%)
USF	1154	234	66	21 (32%)	18 (86%)	3 (14%)	0 (0%)
UWA	1020	790	476	321 (67%)	196 (61%)	19 (6%)	106 (33%)
VMC	1208	404	245	84 (34%)	54 (64%)	7 (8%)	23 (27%)
WFU	1305	536	243	86 (35%)	7 (8%)	4 (5%)	75 (87%)
YRK	1150	-	20	20 (100%)	17 (85%)	1 (5%)	2 (10%)

[3] Number screened based on all patients with completed CRF00
[4] WFS – Withdrawn From Study (post-certification)

Monthly Table 2

Number of Subjects Enrolled/Screened by Month of Participation and Site (past 24 months only)

Month	ALL	UMD	CMC	HOU	WFU	VMC	BMC	AGY	NSD	USF	YRK	MTH	HRV	ESK	PEN	UOK	UWA	SPC	HCM	CAM
Sep 2015	18/82	2/11	1/5	1/5	0/0	1/1	0/3	2/3	1/1	0/0	0/0	2/16	2/7	2/2	0/0	1/3	3/21	0/0	0/1	
Oct 2015	12/85	0/6	1/13	0/6	0/9	0/0	0/3	3/4	0/0	0/1	0/0	1/19	1/2	0/1	0/0	1/4	2/11	0/0	3/6	
Nov 2015	14/83	2/12	0/14	1/10	0/12	0/0	0/1	0/2	0/0	0/3	1/1	0/7	0/2	1/4	0/0	0/3	8/11	0/0	1/1	
Dec 2015	12/91	1/13	1/18	0/6	0/7	0/0	2/3	1/1	0/0	0/0	0/0	0/15	1/2	1/1	1/3	1/3	3/8	0/0	0/0	0/11
Jan 2016	13/74	0/7	0/13	0/7	0/7	0/0	0/4	1/2	0/0	0/1	3/3	2/6	2/3	1/5	1/3	0/2	3/4	0/0	0/1	0/6
Feb 2016	16/68	2/6	0/8	0/5	0/5	0/0	0/2	2/4	0/0	1/4	1/1	1/12	1/2	0/0	1/2	2/2	3/8	0/0	2/4	0/6
Mar 2016	16/83	1/15	0/13	0/1	0/9	0/0	0/9	0/0	0/0	1/1	0/0	2/12	3/4	2/3	2/2	0/1	5/8	0/0	0/1	0/4
Apr 2016	14/81	1/9	0/14	0/0	0/8	0/0	0/1	1/4	0/0	0/0	0/0	2/13	1/2	1/3	0/1	1/1	6/17	0/0	0/1	1/7
May 2016	13/81	1/5	2/18	0/1	0/6	0/0	4/8	0/2	0/0	0/0	0/0	0/9	3/5	0/2	0/0	0/3	2/14	0/0	1/3	0/5
Jun 2016	18/98	2/26	0/12	0/0	0/6	0/0	0/0	1/1	0/0	0/1	0/0	0/10	6/9	0/5	0/7	0/2	9/17	0/0	WFS	0/2
Jul 2016	15/97	2/18	1/14	0/3	0/8	0/9	0/6	0/0	0/0	1/5	0/0	1/9	1/5	0/7	0/0	0/1	9/10	0/0	–	0/4
Aug 2016	15/152	1/16	1/21	0/1	0/20	0/24	0/2	0/2	0/0	1/5	0/0	0/11	2/5	2/8	2/2	0/1	6/34	0/0	–	0/2
Sep 2016	17/126	1/20	1/22	1/1	0/7	0/6	2/6	2/4	0/0	0/0	0/0	0/7	2/6	1/6	0/0	0/0	4/13	0/0	–	2/13
Oct 2016	20/119	1/18	2/20	0/1	0/10	0/11	0/3	1/2	0/0	1/1	0/0	0/11	2/5	1/2	0/0	0/2	12/25	0/0	–	0/3
Nov 2016	22/107	3/17	1/17	3/6	0/8	0/10	2/4	0/1	0/0	2/3	0/0	1/6	4/6	0/5	1/1	0/1	5/11	WFS	–	0/5
Dec 2016	13/87	1/13	1/22	1/3	0/0	0/9	0/1	0/0	1/1	1/3	0/0	0/7	2/3	1/4	0/0	0/0	4/12	–	–	0/1
Jan 2017	7/75	0/18	0/8	1/1	0/9	0/11	0/4	0/0	0/0	0/0	0/0	0/8	0/2	0/2	0/0	0/0	5/9	–	–	0/2
Feb 2017	14/83	0/10	0/19	5/10	0/2	0/5	0/2	1/1	0/0	1/6	0/0	0/3	1/3	0/1	0/1	1/1	5/12	–	–	0/3
Mar 2017	22/92	3/7	0/16	6/10	0/10	0/5	1/2	0/0	0/0	0/1	0/0	0/3	3/5	0/4	0/0	0/0	9/13	–	–	0/5
Apr 2017	18/101	1/16	2/15	6/13	0/0	0/17	0/3	0/1	0/0	1/4	0/0	0/3	1/4	0/4	0/0	0/0	6/10	–	–	0/1
May 2017	52/134	8/24	11/18	9/16	0/0	4/27	0/1	0/0	0/0	0/2	0/0	8/16	0/5	1/4	0/0	0/3	10/15	–	–	0/0
Jun 2017	53/130	8/20	8/19	8/20	0/0	3/14	0/2	0/0	2/2	0/1	0/0	4/16	2/4	1/4	1/1	1/5	13/19	–	–	0/0
Jul 2017	37/105	5/17	8/12	4/14	0/0	2/12	0/1	0/0	0/0	1/3	0/0	7/15	1/7	0/4	0/0	1/6	4/5	–	–	0/0
Aug 2017	50/130	9/19	8/21	2/8	0/0	2/14	0/5	0/0	0/0	0/2	0/0	4/8	0/2	1/5	0/0	0/4	14/15	–	–	0/0
Sep 2017	51/152	14/20	4/10	8/11	0/0	5/15	0/4	0/1	2/2	1/2	0/0	1/9	1/5	1/4	1/1	0/4	1/47	–	–	0/0

Month	ALL	COR	STN	LUB	PSU	MET	DAR	HAC
Sep 2015	18/82							
Oct 2015	12/88							
Nov 2015	14/83							
Dec 2015	12/91							
Jan 2016	13/74							
Feb 2016	16/68							
Mar 2016	16/83							
Apr 2016	14/81							
May 2016	13/51							
Jun 2016	18/99							
Jul 2016	15/97							
Aug 2016	15/152							
Sep 2016	17/126	1/6						
Oct 2016	20/119	0/5						
Nov 2016	22/107	0/6						
Dec 2016	13/97	1/8						
Jan 2017	7/75	1/1						
Feb 2017	14/83	0/4	0/0					
Mar 2017	22/92	0/10	0/1					
Apr 2017	18/101	1/10	0/0					
May 2017	52/134	1/2	1/1					
Jun 2017	53/130	2/3	0/0	0/0	0/0	0/0	0/0	
Jul 2017	37/105	2/5	0/0	1/1	0/0	1/3	0/0	
Aug 2017	50/130	1/4	0/0	3/3	0/0	2/16	2/2	0/0
Sep 2017	51/152	0/0	0/0	5/5	0/1	0/4	0/0	1/1

Monthly Table 3
Number of Expected [5], Completed [6], and Missed [7] Visits by Study Visit
E = Expected, C = Completed, M = Missed

Facility	Enrolled	2 week			3 month			6 month			12 month			Overall		
		E	C	M	E	C	M	E	C	M	E	C	M	E	C	M
ALL	961	884	877 (99%)	2 (0%)	783	732 (93%)	30 (4%)	659	579 (88%)	61 (9%)	560	507 (91%)	17 (3%)	2886	2695 (93%)	110 (4%)
AGY	33	33	33 (100%)	0 (0%)	33	30 (91%)	3 (9%)	31	27 (87%)	4 (13%)	24	22 (92%)	2 (8%)	121	112 (93%)	9 (7%)
BMC	21	19	19 (100%)	0 (0%)	18	18 (100%)	0 (0%)	19	18 (95%)	1 (5%)	17	16 (94%)	1 (6%)	73	71 (97%)	2 (3%)
CAM	3	3	3 (100%)	0 (0%)	3	2 (67%)	1 (33%)	3	2 (67%)	1 (33%)	0	0 (0%)	0 (0%)	9	7 (78%)	2 (22%)
CMC	100	98	98 (100%)	0 (0%)	77	75 (97%)	1 (1%)	58	56 (97%)	2 (3%)	53	52 (98%)	1 (2%)	286	281 (98%)	4 (1%)
COR	10	10	10 (100%)	0 (0%)	8	8 (100%)	0 (0%)	3	3 (100%)	0 (0%)	1	1 (100%)	0 (0%)	22	22 (100%)	0 (0%)
DAR	2	2	2 (100%)	0 (0%)	0	0 (0%)	0 (0%)	0	0 (0%)	0 (0%)	0	0 (0%)	0 (0%)	2	2 (100%)	0 (0%)
ESK	22	21	21 (100%)	0 (0%)	20	17 (85%)	3 (15%)	18	16 (89%)	2 (11%)	17	15 (88%)	2 (12%)	76	69 (91%)	7 (9%)
HAC	1	0	0 (0%)	0 (0%)	0	0 (0%)	0 (0%)	0	0 (0%)	0 (0%)	0	0 (0%)	0 (0%)	0	0 (0%)	0 (0%)
MIN	18	18	18 (100%)	0 (0%)	18	18 (100%)	0 (0%)	18	14 (78%)	1 (6%)	18	15 (83%)	0 (0%)	72	65 (90%)	1 (1%)
HOU	103	94	93 (99%)	0 (0%)	83	75 (90%)	4 (5%)	64	52 (81%)	9 (14%)	51	48 (94%)	2 (4%)	292	268 (92%)	15 (5%)
HRV	72	67	67 (100%)	0 (0%)	64	61 (95%)	3 (5%)	60	54 (90%)	5 (8%)	46	44 (96%)	1 (2%)	237	226 (95%)	9 (4%)
LUB	9	6	6 (100%)	0 (0%)	0	0 (0%)	0 (0%)	0	0 (0%)	0 (0%)	0	0 (0%)	0 (0%)	6	6 (100%)	0 (0%)
MET	3	0	0 (0%)	0 (0%)	0	0 (0%)	0 (0%)	0	0 (0%)	0 (0%)	0	0 (0%)	0 (0%)	0	0 (0%)	0 (0%)
MTH	51	47	46 (98%)	0 (0%)	37	35 (95%)	1 (3%)	25	23 (92%)	2 (8%)	24	22 (92%)	0 (0%)	133	126 (95%)	3 (2%)
NSD	11	10	10 (100%)	0 (0%)	9	9 (100%)	0 (0%)	7	7 (100%)	0 (0%)	6	6 (100%)	0 (0%)	32	32 (100%)	0 (0%)
PEN	15	13	11 (85%)	1 (8%)	13	11 (85%)	1 (8%)	9	8 (89%)	1 (11%)	8	6 (75%)	1 (12%)	43	36 (84%)	4 (9%)
PSU	0	-	-	-	-	-	-	-	-	-	-	-	-	0	0 (0%)	0 (0%)
SPC	10	10	10 (100%)	0 (0%)	10	10 (100%)	0 (0%)	10	10 (100%)	0 (0%)	9	9 (100%)	0 (0%)	39	39 (100%)	0 (0%)
STN	1	1	1 (100%)	0 (0%)	1	1 (100%)	0 (0%)	0	0 (0%)	0 (0%)	0	0 (0%)	0 (0%)	2	2 (100%)	0 (0%)
UKY	8	0	0 (0%)	0 (0%)	0	0 (0%)	0 (0%)	0	0 (0%)	0 (0%)	0	0 (0%)	0 (0%)	0	0 (0%)	0 (0%)
UMD	163	150	150 (100%)	0 (0%)	132	124 (94%)	6 (5%)	115	98 (85%)	17 (15%)	110	99 (90%)	1 (1%)	507	471 (93%)	24 (5%)
UOK	13	11	11 (100%)	0 (0%)	10	10 (100%)	0 (0%)	9	8 (89%)	1 (11%)	8	7 (88%)	1 (12%)	38	36 (95%)	2 (5%)
USF	18	16	14 (88%)	1 (6%)	15	11 (73%)	3 (20%)	14	6 (43%)	6 (43%)	9	6 (67%)	2 (22%)	54	37 (69%)	12 (22%)

[5] A visit is counted as complete (i.e. fully or partially completed) if at least one field in the CRFs to be completed for the visit has been keyed and this visit has not been indicated as missed on AF03. All out of window visits count as completed for the purpose of this report.

[6] A visit is counted as expected when the visit has been completed (as defined above) or when the visit window has been closed for 7 days and no forms have been keyed. Patients who withdraw/ are lost to follow up are kept in as incomplete visits. Deaths are censored at time of death. Patients inappropriately enrolled are removed from all totals. Patients for whom Time Zero (e.g. date of injury) is incomplete are excluded from this report.

[7] A visit is counted as missed based on AF03. Patients with no AF03 or no data entered into REDCap will be listed in Query 2.

Facility	Enrolled	2 week			3 month			6 month			12 month			Overall		
		E	C	M	E	C	M	E	C	M	E	C	M	E	C	M
UWA	196	183	182 (99%)	0 (0%)	164	154 (94%)	1 (1%)	137	121 (88%)	6 (4%)	102	84 (82%)	2 (2%)	586	541 (92%)	9 (2%)
VMC	54	49	49 (100%)	0 (0%)	45	41 (91%)	2 (4%)	36	34 (94%)	2 (6%)	36	35 (97%)	0 (0%)	166	159 (96%)	4 (2%)
WFU	7	7	7 (100%)	0 (0%)	7	6 (86%)	1 (14%)	7	7 (100%)	0 (0%)	7	7 (100%)	0 (0%)	28	27 (96%)	1 (4%)
YRK	17	16	16 (100%)	0 (0%)	16	16 (100%)	0 (0%)	16	15 (94%)	1 (6%)	14	13 (93%)	1 (7%)	62	60 (97%)	2 (3%)

Monthly Table 4
Evaluate Oxygen treatment adherence by Site [8]
By Average Absolute Deviation [9], % Observations Within Range 1 [10] and % Observations Within Range 2 [11]

Facility	Data	Average Absolute Deviation			% of Observations within Range 1			% Observations within Range 2		
		Mean ± SD	Median	Range	Mean ± SD	Median	Range	Mean ± SD	Median	Range
ALL	831	7.3 ± 14.8	3.6	(0.0, 260.0)	75.8 ± 34.1	91.7	(0.0, 100.0)	80.9 ± 32.0	97.0	(0.0, 100.0)
UWA	180	5.6 ± 7.9	3.5	(0.0, 49.4)	84.9 ± 22.8	93.3	(0.0, 100.0)	87.9 ± 21.6	95.5	(0.0, 100.0)
UMD	147	7.9 ± 12.0	4.3	(0.0, 64.0)	79.0 ± 35.3	100.0	(0.0, 100.0)	82.1 ± 32.7	100.0	(0.0, 100.0)
HOU	90	2.2 ± 4.2	1.0	(0.0, 27.1)	52.6 ± 47.9	80.0	(0.0, 100.0)	53.1 ± 48.4	84.6	(0.0, 100.0)
CMC	82	7.8 ± 8.5	4.6	(0.0, 36.2)	74.2 ± 27.5	82.2	(0.0, 100.0)	82.9 ± 25.7	92.3	(0.0, 100.0)
HRV	62	5.1 ± 6.8	2.7	(0.4, 37.4)	81.6 ± 26.0	92.3	(0.0, 100.0)	85.7 ± 25.6	100.0	(0.0, 100.0)
VMC	49	12.3 ± 19.7	5.7	(0.0, 109.8)	62.0 ± 37.3	77.8	(0.0, 100.0)	72.8 ± 34.6	88.2	(0.0, 100.0)
MTH	46	7.9 ± 12.6	3.6	(0.0, 61.4)	69.9 ± 39.3	91.3	(0.0, 100.0)	82.8 ± 30.7	100.0	(0.0, 100.0)
AGY	26	7.7 ± 12.0	2.4	(0.0, 42.8)	76.4 ± 33.6	93.0	(0.0, 100.0)	79.2 ± 33.9	96.9	(0.0, 100.0)
ESK	20	4.8 ± 7.3	1.0	(0.0, 26.6)	87.3 ± 25.4	100.0	(0.0, 100.0)	90.2 ± 22.9	100.0	(0.0, 100.0)
HCM	18	4.9 ± 3.0	4.3	(1.2, 11.9)	90.6 ± 23.7	100.0	(0.0, 100.0)	91.5 ± 23.9	100.0	(0.0, 100.0)
BMC	17	4.0 ± 4.4	2.7	(0.6, 16.7)	91.4 ± 10.9	91.3	(57.1, 100.0)	92.9 ± 11.0	100.0	(57.1, 100.0)
USF	16	4.0 ± 3.1	2.8	(0.9, 10.7)	86.3 ± 14.1	93.5	(56.2, 100.0)	89.8 ± 14.5	98.7	(56.2, 100.0)
YRK	14	6.6 ± 5.9	4.5	(1.5, 18.2)	73.5 ± 40.3	97.6	(0.0, 100.0)	88.9 ± 24.8	100.0	(12.5, 100.0)
COR	10	11.0 ± 21.4	4.6	(0.0, 70.0)	64.0 ± 40.6	76.7	(0.0, 100.0)	75.6 ± 35.9	100.0	(0.0, 100.0)
UOK	10	19.7 ± 47.2	5.3	(1.3, 154.0)	84.7 ± 31.9	98.4	(0.0, 100.0)	87.2 ± 31.6	100.0	(0.0, 100.0)
SPC	9	3.3 ± 3.8	1.2	(0.3, 10.9)	95.7 ± 6.8	100.0	(83.3, 100.0)	96.1 ± 6.7	100.0	(83.3, 100.0)

[8] This table describes adherence to the randomised oxygen concentrations (80% or 90% FiO_2). To preserve blinding, sites with at least 5 patients enrolled are included on this table. There are three sets of means, medians, and ranges in the table. They represent:

[9] Average Absolute Deviation: This set of mean, median, and range measures the distance of each observation recorded on CRF18 from either 90% or 80%, depending on which group the patient was randomised to, and excluding the 1st and last observations recorded. The mean shown here is a mean of the means, and the median is the median of several means. A higher median in this cluster indicates "worse" protocol adherence.

[10] % Observations Within Range 1: This set of mean, median, and range measures the percent of observations recorded on CRF18 that fall within either 80 – 85% or 90 – 95%, depending on which group the patient was randomised to, and excluding the 1st and last observations recorded. This is our more stringent definition of protocol adherence. A higher median in this cluster indicates "better" protocol adherence.

[11] % of Observations Within Range 2: This set of mean, median, and range measures the percent of observations recorded on CRF18 that are < 85% or > 70%, depending on which group the patient was randomised to, and excluding the 1st and last observations recorded. This is our more lenient definition of protocol adherence. A higher median in this cluster indicates "better" protocol adherence.

Table 4 (con't)

Facility	Data	Average Absolute Deviation			% of Obeervations within Range 1			% Observations within Range 2		
		Mean ± SD	Median	Range	Mean ± SD	Median	Range	Mean ± SD	Median	Range
NSD	8	43.9 ± 88.2	7.3	(2.6, 260.0)	54.9 ± 39.7	74.2	(0.0, 90.5)	73.5 ± 38.6	88.6	(4.2, 100.0)
PEN	8	7.9 ± 10.4	1.4	(0.9, 26.2)	67.8 ± 43.7	90.0	(0.0, 100.0)	77.6 ± 34.5	92.6	(0.0, 100.0)
LUB	7	17.0 ± 25.3	7.2	(0.0, 71.8)	62.1 ± 45.1	88.2	(0.0, 100.0)	80.2 ± 36.1	91.7	(0.0, 100.0)
WFU	7	10.4 ± 9.0	7.1	(1.1, 23.5)	71.8 ± 26.1	77.8	(23.1, 100.0)	75.8 ± 28.0	80.0	(23.1, 100.0)

Appendix 3. Oxygen Quad Chart

Supplemental Perioperative Oxygen to Reduce Surgical Site Infection After High Energy Fracture Surgery

OR110123 (W81XWH-12-1-0588)

PI: Robert V. O'Toole, MD **Org:** Department of Orthopaedic Surgery, Univ of Maryland **Award Amount:** $2.447M (Directs only)

Study/Product Aim(s)

Our hypothesis is that the use of supplemental perioperative oxygen for fractures at high risk for infection will reduce infection rates and therefore improve outcomes compared to treatment without this technique.

- **Infection rates will be lower in the treatment arm**
- **There will be no difference in bacterial susceptibilities in the treatment arm**
- **Validate our previous RIOTS model that predicts infection**

Approach

The study uses the DOD-funded METRC infrastructure for a multicenter randomized controlled treatment trial. The study population is patients with high energy tibial plateau, pilon (distal tibia), and calcaneus fractures. The study is guided by a pilot study already completed of 250 fractures at our center. We plan to enroll 1000 patients.

Surgical Site infection (left) in orthopaedic trauma is thought to be affected by biofilm formation (Right). General surgery clinical literature suggests that supplemental perioperative oxygen might limit surgical site infection. The effect on orthopaedic trauma surgery awaits the outcome of this trial.

Accomplishment: We finalized the protocol, CRFs, study sites, and have IRB approval and site certification at 25 sites. 1000 patients have been enrolled with f/u rate of 91% at 1 year. We have revised the goal to add 200 more patients in next 6 months.

Timeline and Cost

Activities CY	13	14	15/16	17/18
Develop and Approve Protocol				
IRB approval at Multiple sites				
Enroll/Follow Patients				
Analysis				
Estimated Budget ($K)	$ 165,127	$741,645	$1,741,138	$0

Updated: (11/06/2017)

Goals/Milestones

Year 1: CY13-14 Goal –Protocol Development/Implementation/IRB

☑ Develop protocol and gain approval of METRC steering committee
☑ IRB approval at METRC Coordinating center and DOD
☑ IRB approval at PI site
☑ Perform site education program for research coordinators
☑ Develop site educational and study materials

Year 2: CY14-15 Goals – Patient enrollment

☑ Begin patient enrollment
☑ IRB/DOD approval at all study sites (24/25 completed to date)

Year 3: CY14-17 Goals – Enrollment completion

☐ Complete patient enrollment & study analysis

Comments/Challenges/Issues/Concerns

• Patient enrollment is >12 months behind due to IRB delays.

Budget Expenditure to Date

Projected Expenditure: $ 785,555 (including JHU sub payments)
Actual Expenditure: $ 1,862,355 (including JHU sub payment)